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Inter-laboratory comparison of xenobiotic clearance rates determined using cryopreserved trout hepatocytes for improving bioaccumulation predictions

Hepatic biotransformation is an important determinant of chemical bioaccumulation in fish. Consequently, bioaccumulation models can be improved using estimates of chemical biotransformation rates. Cryopreserved trout hepatocytes have been used to measure the clearance rates of some compounds, but the transferability of the method has not yet been demonstrated. In this study, three independent laboratories performed a round-robin study using cryopreserved rainbow trout (*Oncorhynchus mykiss*) hepatocytes. Each laboratory conducted clearance assays for six compounds (benzo[a]pyrene, 4-nonylphenol, di-tert butyl phenol, fenthion, methoxychlor and o-terphenyl) using a substrate depletion approach. One compound, o-terphenyl was excluded from the final analyses due to its non-linear behavior and chemical loss in heat-inactivated controls. Compounds determined to be slowly (methoxychlor; $< 0.10 \text{ mL/h/10}^6 \text{ cells}$) or rapidly metabolized (di-tert butyl phenol; $> 0.4 \text{ mL/h/10}^6 \text{ cells}$) were similarly determined across laboratories, following the same rank order (within uncertainty). No compound was found to be metabolically inactive by any laboratory. Coefficients of variation across the three laboratories were between 27 and 61% for measured intrinsic clearance rates, and were further improved by normalization to benzo[a]pyrene. These results strongly support the use of cryopreserved trout hepatocytes in estimating hepatic clearance for bioconcentration factor predictions.